ORIGINAL ARTICLE

A Study of Celiac Disease, Helicobacter pylori Gastritis and Giardiasis in Children with Endoscopic Duodenal Nodularity at a Tertiary Care Centre of Rajasthan.

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ABSTRACT

Introduction: Helicobactor pylori, Celiac disease and Giardiasis are important cause for growth retardation in children. All three conditions can be associated with duodenal nodularity on upper GI endoscopy. Duodenal nodularity is endoscopically determined entity in which visible nodules are seen in the proximal duodenal mucosa. The present study was done to study the occurrence of Celiac disease, Helicobacter pylori gastritis, Giardiasis and their clinical and histopathologic features in pediatric patients with endoscopic duodenal nodularity.

Methods: It was a laboratory based observational study. Duration of the study was one year. Endoscopic biopsies were obtained from 55 pediatric patients and the histopathologic findings were observed after staining with H&E stain and Warthin Starry silver stain.

Results: Of the 55 patients included in the study, the mean age was 9.2 years (range: 1-17 years). Histopathologic examination revealed Helicobacter pylori in 22%, Celiac disease in 18% and Giardiasis in 5% of the patients. Chronic inflammation was observed in all (100%) the patients and villous atrophy in 18% of the patients. The most common presenting symptom was abdominal pain, seen in 40 (74%) patients.

Conclusion: Distinct clinical entities like H.pylori gastritis, Celiac disease and Giardiasis can lead to the development of duodenal nodularity. A proper microbiological and immunologic evaluation should be done in pediatric patients with duodenal nodularity for exact diagnosis and early treatment in order to reduce the associated morbidity.

Keywords: Celiac disease; Duodenal nodularity; Giardiasis; H.pylori

INTRODUCTION

Growth retardation, failure to thrive and developmental delay are the complaints which are commonly faced by children in developing countries like India. Malnutrition still being an important cause of significant mortality and morbidity. Celiac disease, Helicobactor pylori and Giardiasis are important causes for growth retardation in children. All three conditions can be associated with duodenal and antral nodularity on upper GI endoscopy. Duodenal nodularity is an uncommon endoscopic finding characterized by presence of visible nodules ranging from 0.2 to 0.5 cm in diameter in the proximal duodenal mucosa[1,2]. In children duodenal nodularity is a rare finding. Antral nodularity is the most common finding in association with duodenal nodularity[3]. Histopathologically, duodenal nodularity is found to be associated with presence of chronic inflammation, villous atrophy, increase in number of intercryptal and intraepithelial eosinophils[3]. Clinically Celiac disease, Helicobactor pylori gastritis and Giardiasis are found in association with duodenal and antral nodularity[3].

Helicobacter pylori are recognised as one of the most common cause of chronic bacterial, medically important infection affecting the humans worldwide[4]. Helicobacter pylori infection is associated with chronic active gastritis, atrophic gastritis, peptic ulcer disease, mucosa associated lymphoid tissue (MALT) lymphoma and non cardiac gastric cancer[5]. Helicobacter pylori can be demonstrated in hematoxylin and eosin stained section or using special stains like Warthin Starry silver stain,

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Giemsa stain and by immunohistochemistry. On endoscopic examination, H.pylori infection shows nodular appearance of the antral mucosa. The inflammatory infiltrate includes the presence of neutrophils within the lamina propria, including some that cross the basement membrane to assume intraepithelial location and accumulate in lumen of gastric pits to form pit abscesses. Intraepithelial neutrophils and subepithelial plasma cells are characteristic of H.pylori[5].

Celiac disease is an immune-mediated enteropathy which is triggered by ingestion of gluten containing food, such as wheat, rye, or barley, in genetically predisposed individuals[5]. Celiac disease clinically presents with failure to thrive, growth retardation, chronic diarrhea, vomiting, indigestion, delayed puberty and weight loss. Biopsy specimen from second part of duodenum, which is exposed to the highest concentration of dietary gluten, are usually diagnostic of Celiac disease. Celiac disease is characterized by increased intraepithelial lymphocytes, crypt hyperplasia and villous atrophy. Other features include increased number of plasma cells, mast cells and eosinophils, within the upper part of lamina propria[5]. Giardia lamblia is the most common intestinal protozoa worldwide. In India prevalence of Giardia infection in patients with diarrhea ranges from 0.4%-70%[6]. A large majority of individuals infected with Giardiasis remain asymptomatic[7]. Diagnosis of Giardiasis in a duodenal biopsy specimen requires recognition of trophozoites in mucus adjacent to the epithelial surface[8].

The purpose of this study is to evaluate the frequency, spectrum of clinical and histopathologic features of duodenal nodularity in pediatric patients undergoing upper GI endoscopy.

MATERIALS AND METHODS

This laboratory based observational study was conducted on 55 pediatric patients who presented to Pediatric Gastroenterology Department from March 2019 to February 2020 and were found to have duodenal nodularity on upper G.I endoscopy.

Duodenal and antral biopsies were taken from these patients, processed and stained with Hematoxylin and Eosin stain and Warthin Starry silver stain. Inclusion criteria were: Age 1-18 years with endoscopic appearance of duodenal nodularity. Exclusion criteria were: duodenal biopsies from patients without duodenal nodularity and insufficient tissue.

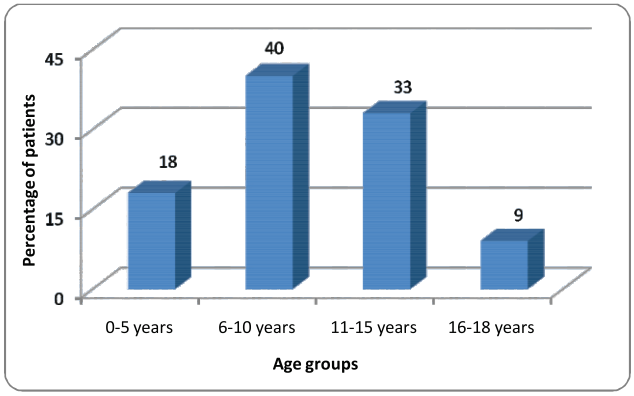
These biopsies were subjected to histopathologic examination. Diagnosis of H.pylori was made on identification of H.pylori on antral mucosa on H&E stain and confirmed with Warthin Starry silver stain. Diagnosis of Celiac disease was made according to criteria of Modified Marsh classification- Oberhuber alongwith serology (anti tTG level) and clinical details. Diagnosis of Giardiasis was made on identification of Giardia on duodenal mucosa. Other clinical findings and histopathologic findings found in these patients were also noted.

Statistical analysis

Occurrence of Helicobacter pylori, Celiac disease, Giardiasis, other histopathologic findings, clinical findings and demographic data was compiled. For continuous data mean, standard deviation and range were calculated. For categorical data, number and percentagewere calculated.

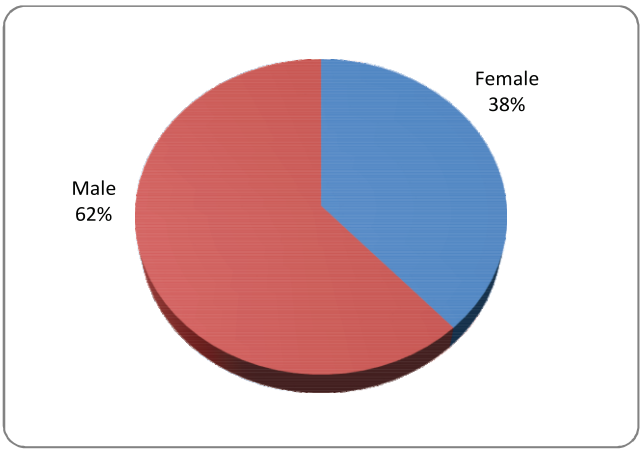
RESULTS

From March 2019 through February 2020, approximately 1000 upper gastrointestinal tract endoscopies were performed in our setting. Nodular duodenum was demonstrated in 55 children (5.5%) endoscopically and all 55 patients were enrolled in our study. There were 34 male (62%) and 21 female (38%) patients with age range of 1-17 years (mean 9.67 ± 4.23). (Graph1)



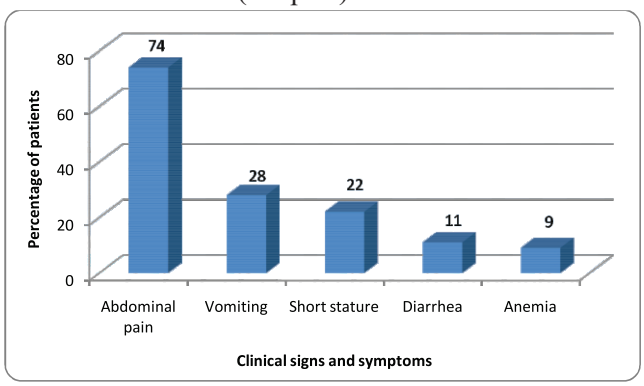
Graph 1: Age distribution of pediatric patients with duodenal nodularity

Most 34(62%) of these patients were males and 21(38%) were females. (Graph 2). The ratio of males to females was 1.62:1.



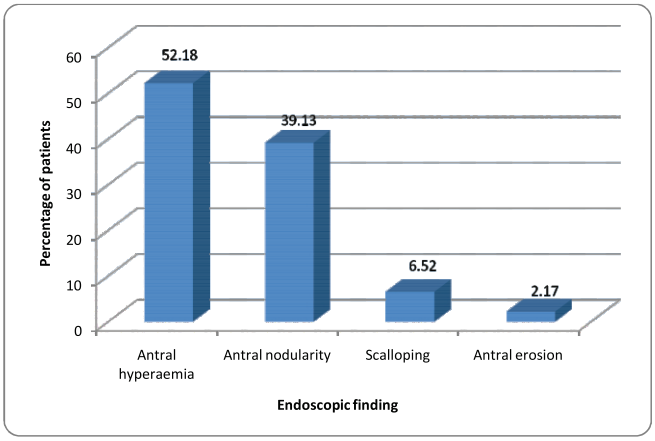
Graph 2: Gender wise distribution of pediatric patients with duodenal nodularity

The most common presenting symptom was abdominal pain, seen in 40 (74%) patients. The clinical features are shown in (Graph 3).



Graph 3: Distribution of patients according to clinical signs and symptoms

Antral hyperaemia (52.18%) was the most common endoscopic finding in children in addition to duodenal nodularity. The endoscopic findings are shown in (Graph 4).

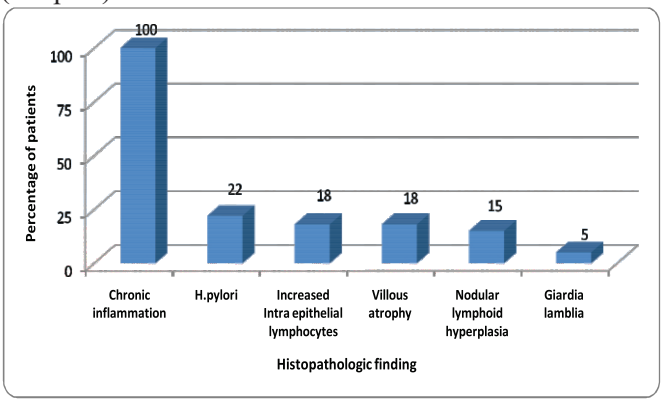


Graph 4: Distribution of patients according to endoscopic findings

Histopathologic evaluation of duodenal nodules revealed chronic inflammatory infiltration ranging from mild to severe in all patients (100%). Gastric biopsy samples were obtained from 39 patients and 12 of them showed Helicobacter pylori on antral mucosal surface. (Graph 5).

Increased intraepithelial lymphocytes and varying degree of villous atrophy were seen in 10 patients (18%), all of them were diagnosed as celiac disease with compatible clinical findings and celiac autoantibody tests. Nodular lymphoid hyperplasia was observed in 8 patients (15%). Giardia lamblia trophozoites were identified on the surface of the duodenal mucosa on histologic examination in 3 patients (5%) (Graph 5). No cases of other protozoal pathogens were identified by light microscopy in our patients.

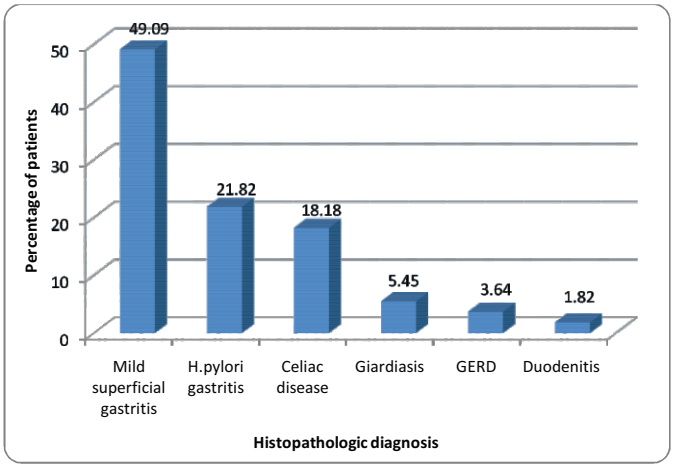
Gastric metaplasia and brunner gland hyperplasia were not seen in our patients. The histopathologic findings of the patients are shown in (Graph 5).



Graph 5: Distribution of patients according to histopathologic evaluation of duodenal nodules

Plasma cells were identified in lamina propria in all biopsies. Well formed granulomas or small collections of histiocytes were not seen. Hyperplastic or adenomatous polyps or any malignant or pre malignant lesions were not identified on histopathologic examination in our patients.

The final histopathologic diagnosis was H.pylori gastritis (Image 1) in 21.82%, Celiac disease (Image 2,3,4) in 18.18% and Giardiasis (Image 5) in 5.45%. (Graph 6)



Graph 6: Distribution of patients according to histopathologic diagnosis

DISCUSSION

Duodenal nodularity is an uncommon endoscopic finding, more so in children and little is known about the pathogenesis of the nodularity. In previous studies, nodular duodenum was seen in certain diseases, such as Celiac disease, H. pylori and Giardiasis. In study conducted by Piazzi et al[9], duodenal nodularity was seen in association with celiac disease. In study conducted by Li et al[10], nodular duodenum was seen in association with Helicobacter pylori and in study conducted by Perez-Roldan et al[11], duodenal nodules were observed in association with giardiasis.

In 1980, Langkemper et al[12], reported radiologic and endoscopic findings of 22 adult patients with nodular appearance of duodenum. They showed histopathologically that all the patients had the characteristic appearance of duodenal bulb caused by heterotopic gastric mucosa except one. Fernandez-Melone et al[13], reported that the incidence of nodular duodenitis was 4% in adult population. They speculated that this appearance was visually distinct, morphologic variant of nonspecific duodenitis. Triadafilopoulos[1] reported the clinical and histopathologic features of 83 male veterans (prevalence 4%) with nodular duodenum and concluded that nodular duodenum might be a variant of duodenitis, probably related with acid-peptic disease and that histopathologic features were variable. All these study groups included adult patients and the prevalence was suggested to be approximately 4%. Gonul et al[3], evaluated the histopathologic features in 17 pediatric patients with nodular duodenum and reported that the prevalence of nodular duodenum was 1.9% in pediatric population. We observed quite a few patients with nodular duodenum and the frequency was 5.5% in our pediatric population.

In studies previously conducted by Piazzi et al[9] and Lee et al[14], it was reported that nodular duodenum was one of the endoscopic markers of celiac disease in adults. Gonul et al[3] reported that the frequency of duodenal nodularity in pediatric celiac patients was 4.6%. In our study there were 10 celiac disease patients with duodenal nodularity and the frequency of celiac disease in patients with endoscopic duodenal nodularity was 18%. So nodular duodenum can be an endoscopic marker of celiac disease in children also. It has also been diagnosed in Giardiasis, intestinal bacterial overgrowth and Celiac disease in adults.

In the present study there were 3 patients with giardiasis. In our study, giardiasis was diagnosed by demonstration of giardia lamblia trophozoites on duodenal mucosa in 3 patients. Although there are no specific histopathologic findings of Giardia infestation, various degrees of villous atrophy, increased intraepithelial lymphocytes count and NLH (Nodular Lymphoid Hyperplasia) were previously described in study by Perz-Roldan et al[11], Vesy et al[15] and Eren et al[16]. Gonul et al[3] described in their study that out of 6 patients with Giardiasis, they observed increased lymphoid infiltration in 5 patients, villous atrophy in 4 and NLH in 3 patients. In our study there was increased lymphoid infiltration in 3 patients and NLH in one patient. Villous atrophy was not seen in our patients with Giardiasis.

NLH, which is defined by heavy infiltration of lymphocyte-resembling lymphoid follicles with germinal center formation, might be a causative explanation of duodenal nodularity. In previous study by Gonul et al[3] NLH was observed in 41% of the patients, not all of them, despite the same appearance in endoscopic examination. Chronic inflammation and IEL infiltration were observed in 100% and 59% of patients respectively. Besides the chronic inflammation, they noticed increased infiltration of eosinophils in the duodenal mucosa in 70.5% of patients. In our study histopathologic findings revealed NLH and increased IEL infiltration in 15% of patients. On the other hand, chronic inflammation was observed in higher frequency (100%) of patients. Lowichik A et al[17] had showed in their study that eosinophilic counts can be naturally higher in pediatric population compared with adults. However, in our study we did not observe increased eosinophilic infiltration in the duodenal mucosa which is contrary to the finding observed by Gonul et al[3]

and Lowichek et al[17]. Geographic differences in the study population may be the reason for the difference in findings. Further investigations are required to support this theory.

Gonul et al[3] in their study had reported 7 (41%) patients with antral nodularity in addition to duodenal nodularity. In our study 18 patients (39%) had antral nodularity in addition to duodenal nodularity. In our study we received gastric biopsy samples from 39 patients, 18 of them had antral nodularity (46%) and found that 12 of them (30%) had H.pylori on antral mucosa. In 6 patients (33%) who had antral nodularity, we observed H.pylori on antral mucosa and 2 patients (11%) had NLH. Gonul et al[3] had previously observed NLH and H.pylori in 100% of patients with antral nodularity. Cohen et al[18] and Ridell RH[19] had suggested previously in their study that there was a very close relationship between H.pylori infection and antral nodular gastritis, particularly in children.

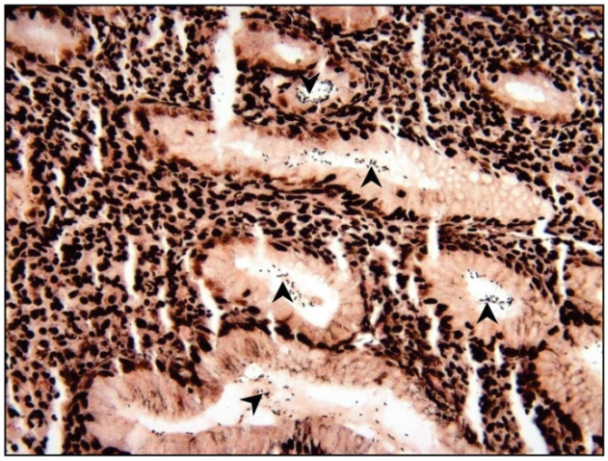


Figure 1: Photomicrograph of antral biopsy showing spiral shaped H.pylori organisms. (Warthin Starry silver stain, 400X)

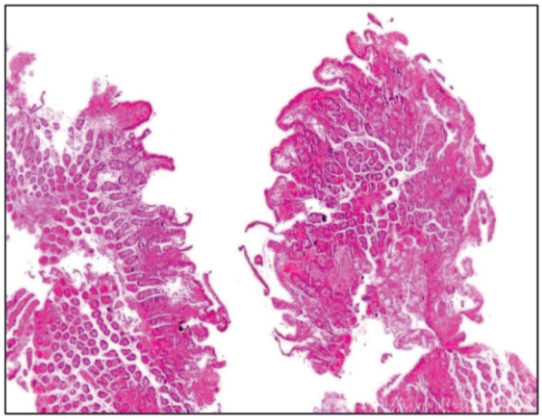


Figure 2: Photomicrograph of D2 biopsy showing mild atrophy of duodenal villi in Celiac disease 3a. (H&E stain, 100X)

CONCLUSION

Endoscopic appearance of duodenal nodularity can be caused by distinct clinical entities like H.pylori gastritis, Celiac disease and Giardiasis. Duodenal nodularity is not associated with any one specific histomorphologic finding. The most demonstrative histomorphologic feature in our study is increased lymphocytic infiltration in duodenal mucosa. A proper microbiological and immunologic evaluation should be done in pediatric patients with duodenal nodularity for exact diagnosis and early treatment in order to reduce the associated morbidity.

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